REMARKS

In view of the following remarks, the Examiner is requested to allow claims 11-15, 17, 18, and 27-38, the only claims pending and under examination in this application.

Claims 11, 12, 27 and 31 have been amended. Support for the amendments can be found in the claims as originally filed and throughout the specification at, for example: original claim 1, and page 6, lines 9-23.

Claim 12 has been amended to clarify that the animal is a rodent. Claim 17 has been amended to add an article. Claim 36 has been amended to replace "cell" with "rodent". Support for these amendments can be found in the specification. These amendments clarify the claims and do not change their scope.

As no new matter has been added by way of these amendments, entry thereof by the Examiner is respectfully requested.

Claim Rejections – 35 U.S.C. § 112, first paragraph

Claims 11-15, 17, 18 and 27-38 have been rejected under 35 U.S.C. § 112, first paragraph on the basis that the specification allegedly does not enable any person skilled in the art to which it pertains, or which it is most closely connected, to make and use the claimed invention commensurate in scope with the claims. The Applicant respectfully traverses this rejection as it applied to the pending claims.

The Examiner acknowledges that enablement is present for a method of inserting an exogenous nucleic acid into the genome of a **mouse**, comprising co-introducing a first nucleic acid sequence encoding a gene of interest operably linked to a promoter, wherein said nucleic acid sequence further comprises a P-element derived recognized insertion sequences and a second nucleic acid sequence encoding a transposase into the testis of said mouse wherein first nucleic acid is inserted into the germline of said mouse and wherein said nucleic acid is transmitted to the offspring.

As the Applicants understand it, the Examiner asserts that the specification does not provide enablement for making any transgenic animal **other than mouse** using any transposon derived insertion sequence commensurate with the scope of the claims.

The law regarding enablement of inventions is clear: "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation."[1]

Claims 11, 13-15, 27 and 31 – "non-human and non-Drosphilidae animal"

Claims 11 and 13-15 are directed to a method of inserting an exogenous nucleic acid into the genome of a **non-human and non-Drosphilidae animal**. Claims 27 and 31 are directed to a **non-human and non-Drosphilidae animal** or cells derived from the animal.

Disclosure of the Present Application

The Applicant maintains that the present application provides sufficient disclosure to enable the invention to the full scope of the pending claims. The present specification clearly details the preparation and production of such transgenic animals. Beginning on page 10, the specification provides a detailed disclosure of how to generate such animals using the transposase recognized insertion sequence vectors and a variety of well known nucleic acid delivery techniques, as well as references describing such techniques in greater detail. Moreover, the specification further provides working examples showing use of such vectors in generating transgenic rodents. Accordingly, the Applicant maintains that the specification fully demonstrates that such non-human and non-Drosophilidae transgenic animals according to the pending claims without practicing undue experimentation.

In addition to standard methods of generating transgenic animals, such as DNA microinjection, at the time the present application was filed methods of overcoming hurdles faced in generating transgenic animals using standard techniques were also well known. For instance methods of using inducible gene expression systems, such as the tetracycline regulateable system for controlling gene function in transgenic animals, and other methods of improving strategies for generating transgenic animals were well documented (see references cited in the Response dated May 4, 2006).

---

1. *United States v. Telectronics, Inc.*, 8 USPQ 2d 1217, 1233 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989). See also *Genentech, Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (Fed. Cir. 1997), *cert. denied*, 522 U.S. 963 (1997); *Scripps Clinic and Research Foundation v. Genentech, Inc.*, 18 USPQ 2d 1001 (Fed. Cir. 1991).

When the Applicant demonstrated that a pair of P-element transposase recognized insertion sequences, which is derived from the Drosophila fly, is able to integrate into the genome of mice, the Applicant succeeded in demonstrating the genetic element of one organism is able to integrate in the genome of an unrelated organism. Both the Drosophila fly and the mouse are classified under the kingdom Animalia; however, the Drosophilia fly is classified under the class Insecta of the phylum Arthropoda while the mouse is classified under the class Mammalia of the phylum Chordata. There is no reason to believe why the genetic element of an organism from one phylum should be capable of integrating into the genome of an organism of another phylum. However, the Applicant has demonstrated this application in the present specification.

At the time the present application was filed, methods of generating transgenic non-human and non-Drosophilidae animals were well known. For example, methods of generating transgenic frog embryos were known (see Exhibit A: Amaya et al., *Methods Mol. Biol.*, 1999, 97:393-414), methods of generating transgenic zebrafish were known (see Exhibit B: Gaiano et al., *Proc. Natl. Acad. Sci. USA*, 1996, 93(15):7777-7782), methods of generating transgenic rats were known (see Exhibit C: Reid et al., *Proc. Natl. Acad. Sci. USA*, 2001, 98(16):9271-9276), methods of generating transgenic rabbit were known (see Exhibit D: Patel et al., *Circulation*, 2001, 104:317-324), and methods of generating transgenic pig were known (see Exhibit E: Miyagawa et al., *J. Biol. Chem.*, 2001, 276(42): 39310-39319); all of which are non-human and non-Drosophilidae transgenic animals.

In addition to standard methods of generating transgenic animals, such as DNA microinjection, at the time the present application was filed methods of overcoming hurdles faced in generating transgenic animals using standard techniques were also well known. For instance methods of using inducible gene expression systems and other methods of improving strategies for generating transgenic animals were well documented (see references cited in the Response dated May 4, 2006).

Accordingly, the Applicant maintains that once transgenesis is demonstrated in one species (mouse) using the P-element derived vectors from such a divergent and unrelated species (Drosophila fly), as detailed in the present specification and described above, it is reasonable to conclude that the methods could be extrapolated to other animals in a similar

manner without undue experimentation. Therefore, once the Applicants demonstrated the possibility of the described method with one species, it is reasonable to conclude that such methods can be used to generate transgenic animals of different species using a vector that comprises a transposase recognized insertion sequence and an exogenous nucleic acid with a reasonable amount of experimentation.

In the "Response to Arguments" section, the Examiner has alleged the Applicant's arguments in the Amendment and Response dated May 4, 2006 are not persuasive. The Applicant disagrees and answers the Examiner's response point by point.

The Examiner alleges that: "The specification has failed to provide guidance as to the sequence of nucleotides present in the exogenous nucleic acid, which will be one that is not found in the genome of the no-human [*sic*] and non-Drosophilidae animals." (page 10). The mechanism for protein synthesis in animal cells is well-known in the art such that one of ordinary skill in the art would have known the nucleotide sequences for expression of any gene of interest in a non-human and non-Drosophilidae animal. As such, the specification need not detail such specific information in order to enable the claimed invention.

The Examiner also alleges that the specification "did not disclose what modifying amounts of DNA based on the weight difference between species were used to create the transgenic rats and fish and therefore failed to provide the skilled artisan with adequate guidance to make and use any of the transgenic non-human and non-Drosophilidae animals." (page 11). Regarding the alleged lack of guidance on what "amounts of DNA" to use for each animal, the specification teaches an example for mice using from 0.5 to 3 µg of transposase vector, thus demonstrating that determining the optimum amount of vector to be used merely requires using a range of different amounts of vector. It is surely within the knowledge of one skilled in the art to use a range of different amounts of vector to introduce into a non-human and non-Drosophilidae animal.

The Examiner cites Dupuy et al. (*Proc. Natl. Acad. Sci. USA*, 2002, 99(7):4495-9) as an example that: "One of skill in the art cannot rely on the on the [*sic*] transgenic art to make such transgenic animal phenotypes" (page 12). The Applicant respectfully disagrees for four reasons. Firstly, Dupuy et al. is irrelevant because the claimed invention is directed to the use of P-element transposase recognized insertion sequences, while Dupuy et al. discloses using

a completely different transposase sequences derived from the *Sleeping Beauty* transposon system. Secondly, the Examiner had not provided any rationale as to why such "position effects" would pose a detriment in the P-element system of the claimed invention. Thirdly, Dupuy et al. themselves offer a simple solution to such "position effects": "The inclusion of insulator elements within the transposon vector may allow more consistent expression of the transgene." (page 4499, left column, first paragraph in the "Discussion" section). Fourthly, Dupuy et al. do not consider the "position effects" is impediment as they state "the SB system may have applications for generating **large numbers of transgenic animals** with simple, single copy insertions of foreign DNA" (page 4499, right column, last paragraph; emphasis added).

Therefore, the Applicants assert that the methods disclosed in the present specification in conjunction with the knowledge available in the art at the time the present application was filed, would enable one of ordinary skill in the art to practice the invention to the full scope of the claims.

In re Wands Factors

In addition to the above, application of the *In re Wands* test to the facts of the present application leads to the conclusion that the presently pending claims are fully enabled, as demonstrated below.

Under *In re Wands*, a determination of enablement requires consideration of eight factors, including: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability or unpredictability of the art; and (h) the breadth of the claims.[2] Accordingly, under *In re Wands*, a determination of enablement is based on the combination of the factors, taken as a whole, not based solely on a single factor.

In the present application, the Applicant further maintains that the specification, coupled with the information known in the art, would enable one skilled in the art to use the invention

---

2. *Ex Parte Forman.*, 230 USPQ 546, 547 (Bd.Pat.App & Interf. 1986); and, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

without undue experimentation. However, in order to provide structure to the Applicant's response, each of the relevant enablement factors is further discussed in detail below.

(a) the unpredictability in the art and the quantity of experimentation necessary

The Applicant notes that the courts have clearly taught that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. For example, see MPEP § 2164.01.[3] Accordingly, the Applicant's citation of *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, in the previous response was to emphasize that where the "experiments are empirical in nature," as in the case of the present application, the court found that no undue experimentation is required.[4]

In citing the research publications the Applicant has sought to establish that the field of generating transgenic mammalian animals is not as unpredictable as stated by Examiner. The publications cited above represent only a small fraction of the total number of publications demonstrating the successful generation of transgenic non-human and non-Drosophilidae animals. Furthermore, the cited research publications establish that in order to make and use the transgenic animal models according to the full scope of the claims in the present application, undue and excessive experimentation would not be required.

The methods disclosed in the cited references used to generate the transgenic non-human and non-Drosophilidae animals were not exactly the same as the method disclosed in the present application. However, the publications have been cited to establish that by reporting the successful generation of non-human and non-Drosophilidae transgenic animal models, the cited publications have substantiated the Applicant's position that the field is not as unpredictable as asserted by the Examiner.

Therefore, since the field is not unpredictable, the fact that the experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation, especially if the experimentation in empirical in nature. Accordingly, the Applicant maintains that the "how to make" and "how to use" requirements of 35 U.S.C. §112, first paragraph, have been fulfilled.

---

3. See also *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 227 USPQ 428 (Fed. Cir. 1985).

As such, the Applicant maintains that the art is replete with successful attempts at generating non-human and non-Drosophilidae transgenic animals. Therefore, the field cannot be as unpredictable and requiring of undue and excessive experimentation as the Examiner stresses. As such, the Applicant respectfully submits that the specification coupled with the information available in the art, at the time the application was filed, would enable one skilled in the art to use the invention without undue experimentation.

(b) the breadth of the claims and the amount of direction or guidance presented

The Applicant argues that the requirement for guidance in the specification shall be taken in conjunction with the guidance available in the art. As noted above, other methods of generating non-human and non-Drosophilidae transgenic animals are disclosed in the art. One skilled in the art of methods involving manipulating DNA and performing cell-based assays would be able to combine the guidance in the disclosure and the guidance available in the art to practice the claimed invention.

Accordingly, the Applicant maintains that the guidance provided in the specification and highlighted in the previous response, when taken in conjunction with the other enablement factors under *In re Wands*, provides the requisite amount of direction and guidance for a person skilled in the art to make and practice the invention to the full scope of the pending claims.

(c) the presence or absence of working examples

The Applicant respectfully notes that under the *In re Wands* factors for determining compliance with the embalmment requirement under Title 35 U.S.C. §112, first paragraph, the presence or absence or working examples is but a single factor to be taken in consideration with the other factors. As such, under *In re Wands*, the presence or absence of working examples is weighed against the other factors, such as the availability in the art of general guidelines relevant to the claimed invention and guidance provided in the specification.

Moreover, the Applicants cite *In re Robbins* and *In re Borkowski* to emphasize that compliance with the enablement requirement under Title 35 U.S.C. §112, first paragraph does

---

4 *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986).

not require or mandate that a specific example be disclosed.[5] Accordingly, the specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art would be able to practice the invention without undue experimentation.[6]

However, as the Examiner notes in the Office Action, the present application does contains at least two working examples demonstrating (1) the creation of transgenic mice using the P-element derived vectors (pages 18-20), and (2) the creation of transgenic mice using the *Sleeping Beauty* derived vectors (pages 21-22). Therefore, the working examples, taken in conjunction with the general guidelines regarding creation of transgenic non-human and non-Drosophilidae animals available in the art and the guidelines disclosed in the specification, provides one skilled in the art adequate enablement to practice the claimed invention.

Accordingly, the Applicant maintains that the present application does enable a person skilled in the art, through the specification as well as the working example, sufficient enablement to apply the teachings in the specification in conjunction with the relevant art to make and use the claimed invention.

(d) the relative skill of those in the art

The Applicant maintains that the present invention involves methods of manipulating DNA and performing cell-based assays. As such, the Applicant notes that the skill level of an artisan, such as a laboratory technician or scientist with experience in molecular biology or the equivalent of a doctoral degree in molecular biology techniques, in using such methods is very high.

For the reasons set forth, the Applicant maintains that the enablement requirement in regards to **non-human and non-Drosphilidae animals** has been met because a) the amount of experimentation required to create a non-human and non-Drosphilidae transgenic animal would not be undue and excessive b) working examples have been provided, c) guidance is given on how to generate and use such animal models, and d) one of skill in the art would be able to perform the experiments as a matter of routine. The specification, therefore, provides

---

5 *In re Robins* 166 U.S.P.Q. 552 (CCPA 1970); *In re Borkowski,* 164 U.S.P.Q. 642 (CCPA 1970).

sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation.

Claims 28 and 32 - "vertebrate"

Claims 28 and 32 are directed to a (non-human) **vertebrate** or cells derived from a (non-human) **vertebrate**.

For the reasons set forth earlier, the Applicant maintains that the present application provides sufficient disclosure to enable the invention to the full scope of the pending claims 28 and 32 in regards to **vertebrates**. The present specification clearly details the preparation and production of such transgenic **vertebrates**. All of the references cited to demonstrate methods of generating transgenic animals provide examples of vertebrates. For example, frogs (Exhibit A: Amaya et al.), zebrafish (Exhibit B: Gaiano et al.), rats (Exhibit C: Reid et al.), rabbits (Exhibit D: Patel et al.), and pigs (Exhibit E: Miyagawa et al.) are all vertebrates.

Vertebrates comprise a subphylum within the phylum of Chordata. The Applicant maintains that once transgenesis is demonstrated in one vertebrate species (mouse) using the P-element derived vectors from such a divergent and unrelated species (Drosophila fly of phylum Arthropoda), it is reasonable to conclude that the methods could be extrapolated to other vertebrates in a similar manner without undue experimentation. Non-mouse vertebrates are genetically and morphologically much more similar to the vertebrate mouse than compared to other non-vertebrate animals. Therefore, once the Applicants demonstrated the possibility of the described method with one species of vertebrate, it is reasonable to conclude that such methods can be used to generate transgenic vertebrates of different species using a vector that comprises a transposase recognized insertion sequence and an exogenous nucleic acid with a reasonable amount of experimentation.

Furthermore, in considering the *In re Wands* factors for the claims directed to vertebrates: In regards to **(a) the unpredictability in the art and the quantity of experimentation necessary**, as demonstrated by the earlier cited research publications, the Applicant has established that the field of generating transgenic vertebrates is not

---

6. *In re Borkowski*, 164 USPQ at 642.

unpredictable as stated by Examiner for non-human and non-Drosophilidae animals. The publications cited above represent only a small fraction of the total number of publications demonstrating the successful generation of transgenic vertebrates. In regards to **(b) the breadth of the claims and the amount of direction or guidance presented**, the breadth of the claims directed to vertebrates is much narrower than the claims directed to non-human and non-Drosophilidae animals. In regards to **(c) the presence or absence of working examples**, the present application contains at least two working examples as directed to the creation of transgenic vertebrates (mice). As explained earlier, **(d) the relative skill of those in the art** is very high.

For the reasons set forth, the Applicant maintains that the enablement requirement in regards to **vertebrates** has been met. The specification, therefore, provides sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation.

Claims 29 and 33 – "mammal"

Claims 29 and 33 are directed to a (non-human) **mammal** or cells derived from a (non-human) **mammal**. The Applicant maintains that the present application provides sufficient disclosure to enable the invention to the full scope of the pending claims 29 and 33 in regards to **mammals**.

For the reasons set forth earlier, the present specification clearly details the preparation and production of such transgenic **mammals**. The references cited earlier to demonstrate methods of generating transgenic animals provide examples of mammals. For example, rats (Exhibit C: Reid et al.), rabbits (Exhibit D: Patel et al.), and pigs (Exhibit E: Miyagawa et al.) are all mammals.

Mammals belong to the class Mammalia of the phylum Chordata. The Applicant maintains that once transgenesis is demonstrated in one mammal species (mouse) using the P-element derived vectors from such a divergent and unrelated species (Drosophila fly of phylum Arthropoda), it is reasonable to conclude that the methods could be extrapolated to other mammals in a similar manner without undue experimentation. Non-mouse mammals are genetically and morphologically very much more similar to mouse than compared to other non-

mammalian animals. Therefore, once the Applicants demonstrated the possibility of the described method with one species of mammal, it is reasonable to conclude that such methods can be used to generate transgenic mammals of different species using a vector that comprises a transposase recognized insertion sequence and an exogenous nucleic acid with a reasonable amount of experimentation.

Furthermore, in considering the *In re Wands* factors for the claims directed to mammals: In regards to **(a) the unpredictability in the art and the quantity of experimentation necessary**, as demonstrated by the earlier cited research publications, the Applicant has established that the field of generating transgenic mammals is not unpredictable as stated by Examiner for non-human and non-Drosophilidae animals. The publications cited above represent only a small fraction of the total number of publications demonstrating the successful generation of transgenic mammals. In regards to **(b) the breadth of the claims and the amount of direction or guidance presented**, the breadth of the claims directed to mammals is very much narrower than the claims directed to non-human and non-Drosophilidae animals. In regards to **(c) the presence or absence of working examples**, the present application contains at least two working examples as directed to the creation of transgenic mammals (mice). As explained earlier, **(d) the relative skill of those in the art** is very high.

For the reasons set forth, the Applicant maintains that the enablement requirement in regards to **mammals** has been met. The specification, therefore, provides sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation.

Claims 12, 17, 30 and 34-37 – "rodent"

Claims 12, 17, 30 and 35-37 are directed to a method of inserting an exogenous nucleic acid into the genome of a **rodent**. Claims 30 and 34 are directed to a **rodent** or cells derived from a **rodent**.

For the reasons set forth earlier, the Applicant maintains that the present application provides sufficient disclosure to enable the invention to the full scope of the pending claims 12, 17, 30 and 35-37 in regards to **rodent**. The present specification clearly details the preparation and production of such transgenic **rodents**. The references cited earlier to

demonstrate methods of generating transgenic animals provide examples of rodents. For example, rats (Exhibit C: Reid et al.) are rodents.

Rodents belong to the order Rodentia of class Mammalia of phylum Chordata. The Applicant maintains that once transgenesis is demonstrated in one rodent species (mouse) using the P-element derived vectors from such a divergent and unrelated species (Drosophila fly of phylum Arthropoda), it is reasonable to conclude that the methods could be extrapolated to other rodents in a similar manner without undue experimentation. Rodents are genetically and morphologically nearly identical to the mouse. Therefore, once the Applicants demonstrated the possibility of the described method with one species of rodent, it is reasonable to conclude that such methods can be used to generate transgenic rodents of different species using a vector that comprises a transposase recognized insertion sequence and an exogenous nucleic acid with a reasonable amount of experimentation.

Furthermore, in considering the *In re Wands* factors for the claims directed to rodents: In regards to **(a) the unpredictability in the art and the quantity of experimentation necessary**, as demonstrated by the earlier cited research publications, the Applicant has established that the field of generating transgenic rodents is not unpredictable as stated by Examiner for non-human and non-Drosophilidae animals. The publications cited above represent only a small fraction of the total number of publications demonstrating the successful generation of transgenic rodents. In regards to **(b) the breadth of the claims and the amount of direction or guidance presented**, the breadth of the claims directed to rodents is exceedingly much narrower than the claims directed to non-human and non-Drosophilidae animals. In regards to **(c) the presence or absence of working examples**, the present application contains at least two working examples as directed to the creation of transgenic rodents (mice). As explained earlier, **(d) the relative skill of those in the art** is very high.

For the reasons set forth, the Applicant maintains that the enablement requirement in regards to **rodents** has been met. The specification, therefore, provides sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation.

Claims 18 and 38 – "mouse"

Claims 18 and 38 are directed to a method of inserting an exogenous nucleic acid into the genome of a **mouse** by introducing into the mouse a P-element derived vector comprising the exogenous nucleic acid under conditions sufficient for transposition to occur so that said exogenous nucleic acid is inserted into the genome. The Examiner has stated that the present specification enables a method of inserting an exogenous nucleic acid into the genome of a **mouse**. The Examiner has not provided any reasoning as to why the claimed method is not enabled in regards to mouse. For the reasons set forth earlier, the Applicant maintains that the present application provides sufficient disclosure to enable the invention to the full scope of the pending claims 18 and 38 in regards to **mouse**.

As such, for at least the reasons described above, claims 11-15, 17, 18 and 27-34 are adequately enabled by the specification. Accordingly, the Applicants respectfully request that the rejection of claims 11-15, 17, 18 and 27-34 under 35 U.S.C. §112, first paragraph be withdrawn.

Claim Rejections – 35 U.S.C. § 103

Claims 27-34 have been rejected under 35 U.S.C. § 103(a), for allegedly being rendered obvious by Clough et al., *Mol. Cell. Biol.* 5(4):898-901 (1985) in view of Rio et al., *J. Mol. Biol.* 200:411-415 (1988), or Rio et al., *Cell* 44:21-32 (1986), or Rio, *TIG* 7:282-287 (1991). In view of the following remarks, this rejection should be withdrawn.

The present claims are directed to **a non-human and non-Drosophilidae animal or cells derived from the animal** that has P-element transposase recognized insertion sequences integrated into the genome.

The law is clear that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones,* 21 USPQ2d 1941 (Fed. Cir. 1992). Second, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 231 USPQ 375 (Fed. Cir. 1986). Finally, **the**

prior art reference, or references when combined, must teach or suggest all the claim limitations. *In re Royka*, 180 USPQ 580 (CCPA 1974).

The Applicant respectfully contend that the Examiner has failed to establish a *prima facie* case of obviousness, because the cited references do not teach or suggest the claim element of "**a non-human and non-Drosophilidae animal or cells derived from the animal**". The combined teaching of the cited references fails to teach or suggest **a non-human and non-Drosophilidae animal or cells derived from the animal** that have a P-element transposase recognized insertion sequences integrated into the genome. None of the cited references teach or suggest this claim element.

Clough et al. discloses introducing a gene transfer vector into mouse LTV$^-$ cells in plastic tissue dishes (page 898, left column, bottom paragraph). Rio et al. (1988) disclose transfecting a plasmid containing P element transposase sequences into cultured monkey kidney cells (page 411, right column, bottom paragraph). Rio et al. (1986) disclose transfecting Drosophila Schneider line-2 cells (page 29, right column, "Cell Culture and DNA Transformation"). Rio (1991) reviews P element transposition in Drosophila. In fact, the teaching of all the cited references is directed to cells in culture or Drosophila. The Examiner has not shown where the cited references teach **a non-human and non-Drosophilidae animal or cells derived from the animal**. None of the cited references, alone or in any combination, provide for insertion of a transposase sequence into the genome of an animal.

The Examiner alleges that "Rio et al. teaches that P elements will be good genetics tools to use in other organisms where classical genetics is tedious." (page 13). It is not clear to which Rio et al. reference the Examiner is referring to, and where within the reference that this teaching could be found. The Applicant respectfully contends none of the cited Rio references contain such a teaching.

Of the three Rio references[7], the earliest, Rio et al. (1986), discloses that: "Preliminary results . . . suggest that functional P element transposase can be expressed in cultured mammalian cells [and this] raises the **possibility** of using modified P elements as vectors for transformation of organisms other than Drosophila." (page 29, left column, "Transposase

7 All of the Rio references are authored by the same person, Donald C. Rio, at the Department of Biochemistry, University of California, Berkeley, and later The Whitehead Institute for Biomedical Research, M.I.T.

Expression May Allow P Element Transposition in Other Species"; emphasis). Two years later, Rio et al. (1988) teach away from using the P element in a non-human and non-Drosophilidae animal or cells derived from the animal, in that Rio et al. (1988) disclose: "Our results do not exclude the possibility that P elements may be useful as universal transformation vectors, but do indicate that **our present level of understanding is insufficient** to achieve this goal." (page 414, right column, last paragraph; emphasis added). The most recent Rio reference, Rio (1991), does not at all teach or suggest using P elements in any organism other than Drosophila. Clearly, there is no teaching or suggestion of the claim element "a non-human and non-Drosophilidae animal or cells derived from the animal".

Accordingly, these references fail to teach or suggest the claimed invention and this rejection should be withdrawn.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number TOSK-007CIPCON.

Respectfully submitted,

BOZICEVIC, FIELD & FRANCIS LLP

Date: October 27, 2006

By: _____
Robin C. Chiang, Ph.D.
Registration No. 46,619

Date: 10.27.06

By: _____
Bret E. Field
Registration No. 37,620

Enclosure:

- Exhibit A: Amaya et al., *Methods Mol. Biol.*, 1999, 97:393-414
- Exhibit B: Gaiano et al., *Proc. Natl. Acad. Sci. USA*, 1996, 93(15):7777-7782
- Exhibit C: Reid et al., *Proc. Natl. Acad. Sci. USA*, 2001, 98(16):9271-9276
- Exhibit D: Patel et al., *Circulation*, 2001, 104:317-324
- Exhibit E: Miyagawa et al., *J. Biol. Chem.*, 2001, 276(42): 39310-39319

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, California 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

F:\DOCUMENT\Tosk\007cipcon\ROA of 7-31-06.doc